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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/823,152	04/12/2004	Philip A. Carpino	PC25808A	4558

28523 7590 04/16/2008

PFIZER INC.
PATENT DEPARTMENT, MS8260-1611
EASTERN POINT ROAD
GROTON, CT 06340

EXAMINER	
DESAI, RITA J	

ART UNIT	PAPER NUMBER
1625	

NOTIFICATION DATE	DELIVERY MODE
04/16/2008	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

~IPGSGro@pfizer.com

Office Action Summary	Application No.	Applicant(s)	
	10/823,152	CARPINO ET AL.	
	Examiner	Art Unit	
	Rita J. Desai	1625	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,4,8-11,31,35,36,42,43,49,55,59 and 64* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1, 4, 8-11, 31, 35, 36, 42, 43, 49, 55, 59 and 64* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *3/20/08*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 3/20/08 has been entered.

Claims pending 1, 4, 8-11, 31, 35, 36, 42, 43, 49, 55, 59 and 64.

The claims have been amended to a certain extend.

The rejection of the claims 1, 4, 8-11, 31, 35, 36, 42, 43, 49, 55, 59 and 64 under 35 USC 112 still stands.

Applicants argue that the examiner has not provided any evidence that their compounds are not enabled . This is incorrect and it is explained further below.

Applicants also argue that their compound was assayed along side SR141716A as a CB1 antagonist , which is a known compounds to treat obesity and hence its (applicants invention) activity is the same.

It should be noted that SR141716A was approved by FDA in 2006, long after applicants had filed their invention. Thus at the time the invention was made the activity was not known.

Secondly the SR141716A has now been taken off the market because of the increased side effects. See the article from Wikepedia attached.

Despite the FDA issuing an approvable letter in February 2006 for the obesity indication and a non-approvable letter for smoking cessation, the drug did not enter the market in the United States in 2006. The French pharma firm Sanofi-Aventis disclosed that a complete response to the FDA's approvable letter was submitted on October 26, 2006, triggering a Class I (two-month) or Class II (six-month) review process. On June 13, 2007, FDA's Endocrine and Metabolic Drugs Advisory Committee (EMDAC) concluded that the French manufacturer Sanofi-Aventis failed to demonstrate the safety of rimonabant and voted against recommending the anti-obesity treatment for approval.[2] Subsequently, Sanofi-Aventis announced that it was withdrawing the new drug application (NDA) for rimonabant and that it would resubmit an application at some point in the future.

At the time of the invention , applicants had not shown that the compounds can treat obesity.

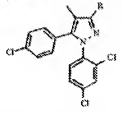
The state of the art is such that that drug did not enter the market and a review is still to be conducted.

Even in 2005 " Current Knowledge on the Antagonists and Inverse Agonists of Cannabinoid Receptors" by Muccioli et al teaches numerous similar compounds and it does not have any teaching of them treating obesity.

Table 4 , page 1366 , teaches compounds similar to SR141716 with a slight different in the substitutent "R" and the activity of the compounds change from inverse antagonist to neutral antagonist.

Table 4. CB_1 Cannabinoid Receptor Antagonists: 3. Diaryl-Pyrazole Derivatives. Five SR141716A (14) Derivatives Illustrating the Importance of the C-3 Carboxamide Oxygen in the SR141716A Inverse Agonism

The structure, affinity ($[^3H]$-SR141716A, hCB_1-HEK293 cells), and function (Ca^{++} mobilization) are given for each compound.



Cpd.	n°	R=	Affinity	Function	References
SR141716A	14		Ki=2.3nM	Inverse agonist	[67]
VCHSR1	15		Ki=31.3nM	Neutral antagonist	[67]
CHASR1	16		Ki=1.7nM	Inverse agonist	[68]
CHMSR1	17		Ki=29nM	Inverse agonist	[68]
PPSR1	18		Ki=261nM	Neutral antagonist	[68]
PIMSR	19		Ki=6.7nM	Neutral antagonist	[68]

Thus the art is very unpredictable with respect to the structure of the compounds and the also the activity.

In view of this unpredictability , applicants should have provided more that these compounds drawn to the full scope as claimed , do posses the property of treating obesity.

The examiner is maintaining the rejection and is repeating here for convenience.

The rejection of the claims 1-4, 7-11, 30, 31, 34-36, 42, 43, 49, 55 , 59 and 64 under 35 USC 112 first paragraph scope of enablement still stands.

Applicants arguments are not found to be convincing.

The various generic substitutents are so varied and the chemical and pharmaceutical art is highly unpredictable and applicants have not provided guidance on how to make these compounds and also to use them commensurate to the scope of the claimed compounds.

The rejection is being repeated and still stands.

Claims 1-4, 7-11, 30, 31, 34-36, 42, 43, 49, 55, 59 and 64 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for compounds wherein R1 and Ro are aryl (phenyl) with halogen or methoxy substitutents, or R4 to be an alkyl, halogen substituted alkyl or a cycloalkyl,

does not reasonably provide enablement for R1, Ro or R4 to be a hetero aryl or have other substitutents or any chemical moiety selected from alkyl, 3to 8 membered partially or fully saturated carbocyclic ring or 3-6 membered partially of fully saturated heterocyle, aryl, heteroaryl, wherin the chemical moiety is again optionally substituted. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

In re Wands, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988).

There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is "undue". These factors include 1) the breadth of the claims, 2) the nature of the invention, 3) the state of the prior art, 4) the level of one of ordinary skill, 5) the level of predictability in the art, 6) the amount of direction provided by the inventor, 7) the existence of working examples, and 8) the quantity of experimentation needed to make or use the invention based on the content of the disclosure. In re Wands, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988).

1) The breadth of the claims: The instant claims encompass many thousands of compounds from an aromatic carbocyclic moiety to an aromatic carbocyclic moiety having many large electron withdrawing and bulky groups substituted on it to a moiety having many heterocyclic rings. These compounds cover a very wide range of compounds.

2) The nature of the invention: The invention is drawn to compound used to treat diseases

3) The state of the prior art:

How to Use:-

The state of the prior art is that the drugs and the enzymes react in a lock and key mechanism and the structure of the compound has to be specific. Even a difference of a methyl group verses a hydrogen changes the properties altogether. A good example is a theophylline verses caffeine. They differ by just a methyl group but one of them has a pharmaceutical use as a bronchodilator. There is no absolute predictability and no established correlation between the different substitutions on a core that they would all behave in the exact same way.
Also again the state of the prior art is that it involves screening in vitro and invivo to determine which compounds exhibit the desired pharmacological activities. There is no absolute predictability and no established correlation between in vitro activity and the treatment diseases is not a reliable predictor of success even in view of the seemingly high level of skill in the art.
The existence of these obstacles establishes that the contemporary knowledge in the art would prevent one of ordinary skill in the art from accepting any therapeutic regimen on its face.

How to make :-

Any chemist would know that it is not a quick and easy way of synthesizing compounds.
As stated in the preface to a recent treatise:
"Most non-chemists would probably be horrified if they were to learn how many attempted syntheses fail, and how inefficient research chemists are. The ratio of successful to unsuccessful chemical experiments in a normal research laboratory is far below unity, and synthetic research chemists, in the same way as most scientists, spend most of their time working out what went wrong, and why. Despite the many pitfalls lurking in organic synthesis, most organic chemistry textbooks and research articles do give the impression that organic reactions just proceed smoothly and that the total synthesis of complex natural products, for instance, is maybe a labor-intensive but otherwise undemanding task. In fact, most syntheses of structurally complex natural products are the result of several years of hard work by a team of chemists, with almost every step requiring careful optimization. The final synthesis usually looks quite different from that originally planned, because of unexpected difficulties encountered in the initially chosen synthetic sequence. Only the seasoned practitioner who has experienced for himself the many failures and frustrations which the development (sometimes even the repetition) of a synthesis usually implies will be able to appraise such work .....Chemists tend not to publish negative results, because these are, as opposed to positive results, never definite (and far too copious) ....." Dorwald F. A.
Side Reactions in Organic Synthesis, 2005, Wiley: VCH, Weinheim pg. IX of Preface

The availability of the starting material that is needed to prepare the invention as claimed is at

issue here.. As per MPEP 2164.01 (b):
A key issue that can arise when determining whether the specification is enabling is whether the starting materials or apparatus necessary to make the invention are available. In the biotechnical area, this is often true when the product or process requires a particular strain of microorganism and when the microorganism is available only after extensive screening. The Court in In re Ghiron, 442 F.2d 985, 991,169 USPQ 723, 727 (CCPA 1971), made clear that if the practice of a method requires a particular apparatus, the application must provide a sufficient disclosure of the apparatus if the apparatus is not readily available. The same can be said if certain chemicals are required to make a compound or practice a chemical process. In re Howarth, 654 F.2d 103, 105, 210 USPQ 689, 691 (CCPA 1981).

4) The level of one of ordinary skill: The ordinary artisan is highly skilled.

5) The level of predictability in the art: It is noted that the pharmaceutical art is unpredictable , requiring each embodiment to be individually assessed for physiological activity. In re Fisher, 427 F. 2d 833, 166 USPQ 18(CCPA 1970) indicates that the more unpredictable an area is, the more specific enablement is necessary in order to satisfy the statue. The level of unpredictability is in the art is very high. The compounds which differ by a methyl group also show different properties, for e.g. theophylline and caffeine. One of them is a bronchodilator and they differ only by a methyl group.
See *In re Fisher*, 166 USPQ 18, at 24 (In cases involving unpredictable factors, such as most chemical reactions and physiological activity, the scope of enablement obviously varies inversely with the degree of unpredictability of the factors involved.), *Nationwide Chemical Corporation, et al. v. Wright, et al.*, 192 USPQ 95 (one skilled in chemical and biological arts cannot always reasonably predict how different chemical compounds and elements might behave under varying circumstances), *Ex parte Sudilovsky* 21 USPQ2d 1702 (Appellant's invention concerns pharmaceutical activity. Because there is no evidence of record of analogous activity for similar compounds, the art is relatively unpredictable) *In re Wright* 27 USPQ2d 1510 (the physiological activity of RNA viruses was sufficiently unpredictable that success in developing specific avian recombinant virus vaccine was uncertain).

6) The amount of direction provided by the inventor: The inventor provides very little direction in the instant specification. There are no examples with the R1, R0 or R4 being hetero cyclic groups nor are there any examples with them having other substitutents or any chemical moiety selected from alkyl, 3to 8 membered partially or fully saturated carbocyclic ring or 3-6 membered partially of fully saturated heterocyle, aryl, heteroaryl, wherin the chemical moiety is again optionally substituted. and also there is no data provided to show that these compounds do indeed treat obesity .

7) The existence of working examples: The instant specification does not have any working examples commensurate to the scope of the claims.

Even the starting materials needed to make these compounds commensurate with the scope, are not provided .

8) The quantity of experimentation needed to make or use the invention based on the content of the disclosure: Since there are no working examples, and the direction given is so little , it would require an undue amount of experimentation to make and use the compounds of the invention.

Taking the above eight factors into consideration, it is not seen where the instant specification enables the ordinary artisan to make and/or use the instantly claimed invention.

Genetech Inc Vs Nova Nordisk 42 USPQ 2d 1001.

"A patent is not a hunting license. It is not a reward for search but compensation for its successful conclusion and patent protection is granted in return for an enabling disclosure of an invention , not for vague intimations of general ideas that may or may not be workable."

MPEP 2164.01(a) states, "A conclusion of lack of enablement means that, based on the evidence regarding each of the above factors, the specification, at the time the application was flied, would not have taught one skilled in the art how to make and/or use the full scope of the claimed invention without undue experimentation. In re Wright, 999 F.2d 1557,1562, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993)." That conclusion is clearly justified here. Thus, undue experimentation will be required to practice Applicants' invention.

New Rejections:-

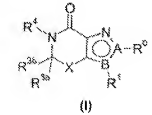
Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

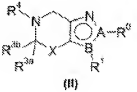
A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1, 4, 8-11, 31, 35, 36, 42, 43, 49, 55, 59 and 64 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-23 of U.S. Patent No. 723024. Although the conflicting claims are not identical, they are not patentably distinct from each other because they are drawn to a similar core.



(I)

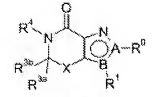


(II)

wherein X is a bond and A is N and B is C. These compounds have a similar activity.

Claims 1, 4, 8-11, 31, 35, 36, 42, 43, 49, 55, 59 and 64 rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-18 of U.S.

Patent No. 7241788. Although the conflicting claims are not identical, they are not patentably distinct from each other because they are drawn to the same core.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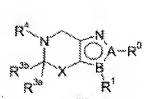
(II)

Claims 1, 4, 8-11, 31, 35, 36, 42, 43, 49, 55, 59 and 64 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-16 of U.S. Patent No. 7141669 and claims 1-17 of US 7145012. Although the conflicting claims are not identical, they are not patentably distinct from each other because in view of the other patents above and with the close similarity in the structure, and the teaching that X can be a bond, one highly skilled in the art such as the inventor would have been motivated to make the modifications to obtain the invention of the instant application.

Conclusion

Claims 1, 4, 8-11, 31, 35, 36, 42, 43, 49, 55, 59 and 64 are rejected.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Rita J. Desai whose telephone number is 571-272-0684. The examiner can normally be reached on Monday - Friday, flex time..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Janet Andres can be reached on 571-272-0867. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Rita J. Desai
Primary Examiner
Art Unit 1625

R.D.
April 11, 2008

/Rita J. Desai/
Primary Examiner, Art Unit 1625